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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/601,656	06/20/2003	Bill E. Cham	13131-0310 (44378-282108)	8075
23370	7590	09/26/2005	EXAMINER CHEN, STACY BROWN	
JOHN S. PRATT, ESQ KILPATRICK STOCKTON, LLP 1100 PEACHTREE STREET ATLANTA, GA 30309			ART UNIT	PAPER NUMBER 1648

DATE MAILED: 09/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/601,656	CHAM ET AL.	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 20 July 2005.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1,2,28-31 and 33-47 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1,2,28-31 and 33-47 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 20 June 2003 is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. 10/311,679.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. Applicant's amendment filed July 20, 2005 is acknowledged and entered. Applicant cancelled claim 32, for which a restriction was made mid-prosecution on June 24, 2005. A restriction was required because claim 32 presented multiple sequences for examination. The examiner restricted between the sequences. Claim 32 has been cancelled in the amendment of July 20, 2005 and prosecution on the merits will continue for the pending claims. Claims 1, 2, 28-31 and 33-47 are pending and under examination. Claims 28-31 and 33-47 have not been treated on the merits prior to this Office action because they were presented after the first Office action, and because of the necessity of a restriction mid-prosecution. Since this application has received an Office action on the merits and the original and newly presented claims remain rejected, this Office action is final.

Applicant is reminded that the embodiments of hepatitis and pestivirus in the claims are directed to non-elected subject matter. Should linking claim 1 be found allowable, the eligible non-elected embodiments will be examined on the merits.

Claim Objections

2. Claim 34 is objected to for improper grammar. In particular, "wherein one or more protein" should be "wherein one or more proteins".

Claim Rejections - 35 USC § 112

3. The rejection of claims 1, 2 and 28-47 under 35 U.S.C. 112, second paragraph, is moot with respect to cancelled claim 32, and withdrawn with respect to claims 1, 2, 28-31 and 33-47.

The rejection was based on the grounds that “a partially delipidated viral particle” is unclear with respect to the term “partially”. Upon further consideration, one of skill in the art would recognize that the claimed viral particle is not completely delipidated, nor is it in its natural state. Therefore, while the term is broad, it is not indefinite.

4. Claims 39 and 40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The limitation in claim 39 and dependent claim 40, “the at least one immunoreactive protein” lacks antecedent basis in claim 1. It appears that Applicant intends for claim 39 to depend from claim 38.

5. Claims 2, 28-31, 37, 39 and 40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. Previously, only claim 2 was rejected, however, claims 28-31, 37, 39 and 40 were added in the amendment filed April 11, 2005 and have not been examined on the merits until this Office action. Claims 28-31, 37, 39 and 40 are drawn to embodiments of immunodeficiency viruses. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

Applicant’s arguments have been carefully considered but fail to persuade. Applicant’s substantive arguments are primarily directed to the following:

- Applicant argues that the specification describes the process of delipidating HIV and SIV particles. Applicant points to the immune response in mice upon administration of the delipidated viral particles.
 - In response to this argument, one of skill can make the viral particles, however, one cannot induce protection against HIV. While it is possible to make a delipidated particle, one cannot make a delipidated particle that protects against HIV infection.
- Applicant argues that the lack of immunodeficiency vaccines does not indicate a lack of enablement for Applicant's invention as claimed. Rather, it demonstrates the novelty and non-obviousness of the instant invention.
 - In response to this argument, consideration of the state of the art is a factor in the enablement analysis. The factors include the breadth of the claims, the nature of the invention, the state of the art, the level of skill and predictability in the relevant art, etc. The examiner has considered the factors with respect to the HIV vaccine claims. Based on those factors, including the state of the art, the examiner has concluded that the claims are not enabled. This analysis has legal basis.
- Applicant argues that the Desrosiers reference (*Nature Medicine*, 2004, 10:221-223) teachings are not indicative of the instant invention's claims. Desrosiers teaches that the natural immune response to HIV is not adequate to protect from HIV infection. Applicant argues that the instant particles are not equivalent to natural HIV.

- In response, the Desrosiers reference is used as evidence of the state of the art.

The state of the art is that a natural immune response to HIV is not sufficient to overcome an infection. This is an important consideration for any vaccine. If the immune system is able to mount its own defense, then a vaccine would be easier to make. However, HIV is not readily defended by the human immune system, thus making the HIV vaccine effort very difficult.

- Further, Applicant has not shown protection via challenge experiments in an acceptable animal model. For viruses such as HIV that mutate rapidly and evade the immune system, challenge experiments in acceptable animal models is required to demonstrate protection.
- Applicant argues that the variability of sequences among HIV-1 isolates is not material to the instant invention's enablement. Applicant argues that epitopes are already present on the delipidated viral particles. Thus, any difficulty in mapping epitopes is not a factor in the instant invention.
 - In response to this argument, the variability of the HIV-1 isolates is part of the enablement analysis, showing the state of the art and the level predictability in the art. While Applicant is not constructing epitopes individually, the process of delipidation is known to alter the epitopes. Applicant is claiming that the delipidated virus particles exhibit hidden epitopes. Epitopes on the surface of the virus or on the interior are expected to change rapidly. Therefore, knowledge of the variability of epitopes is important for assessing the level of predictability in the art, which in this case is very low.

- Applicant argues that the SHIV and SIV animal models are acceptable animal models for HIV. Applicant argues that the SHIV model is reasonably correlated with HIV in humans.
 - In response this argument, while SHIV and SIV models may be the closest model with a correlation to HIV, no instances of protection in macaques has been met with success at the clinical level. The state of the art is that peptide vaccines are unsuccessful. Since Applicant's "vaccine" comprises incomplete viral particles, one of skill in the art would not expect it to protect humans against HIV-1 challenge.
- Applicant argues that responses in animal models are adequate for enabling an HIV-1 vaccine for humans.
 - In response to this argument, the animal models for HIV-1 have not proven effective *in vivo* in humans. While results in animals may look promising, the truth is that humans have not been protected with immunogens against HIV in any way. There is not one success story about protection of humans against HIV-1.
 - Applicant has not demonstrated protection in monkeys. If Applicant had demonstrated protection in monkeys, such evidence would be more convincing. However, there is not data with regard to protection in monkeys in the instant specification.
 - Given the knowledge of the state of the art regarding HIV-1 vaccines and the lack of adequate data presented in the specification, one of skill in the art would not

expose themselves or anyone else willing to HIV-1 after having been injected with Applicant's composition.

- Applicant also argues that the instant composition is enabled for a therapeutic or a pharmacological utility.
 - In response, Applicant's claims are not drawn to therapeutic or pharmacological uses. The claims are limited to protection. Regardless, therapeutic and pharmacological compositions must confer beneficial results. The instant composition is enabled for inducing an immune response, however, any therapeutic or pharmaceutical utility for an HIV-1 viral particle must be backed with evidence of beneficial results in an acceptable animal model.

Claim Rejections - 35 USC § 102

6. Claims 1, 2, 28-31 and 33-47 are rejected under 35 U.S.C. 102(b) as being anticipated by Naficy (US Patent 5,419,759, cited on the IDS filed June 20, 2003). The claims are drawn to a modified immunodeficiency virus particle comprising at least a partially delipidated immunodeficiency virus particle that initiates a positive immune response in an animal or human patient and incites protection against an infectious organism. (The infectious organism is understood to be the same species (HIV, SIV, FIV, etc.) as the delipidated viral particle.) The specification indicates that the viral particle is modified by exposing a non-delipidated viral particle to a delipidation process wherein the lipid content of a virus is reduced. The particle is not infectious, yet remains immunogenic and exposes epitopes that are not usually presented to the immune system by untreated virus. The virus particle proteins are structurally changed by

the delipidation process on, in or near the surface of the virus (page 20, lines 10-23). Particular epitopes include gag, p6, gp66, gp41, p27 or env. The modified viral particle retains over 90% of major protein constituents. *This rejection is based solely on the claimed components, not the uses thereof (protection via vaccination).*

Naficy discloses a method of treating HIV comprising an apheresis method that treats HIV infected components of a patient's blood with diethyl ether to kill infected cells and destroy the lipid envelope of the virus. The patient's blood containing delipidated virus (substantially free of the ether) is then returned to the patient (abstract and col. 9, lines 12-47). Since the particles of Naficy are made by the exposure to an ether, as are Applicant's modified particles, the viral particles of Naficy are delipidated and therefore anticipate the instant claims.

Applicant's arguments have been carefully considered but fail to persuade. Applicant's substantive arguments are primarily directed to the following:

- Applicant argues that Naficy's method destroys the lipid envelope of HIV, rendering the virus unable to penetrate and infect healthy cells.
 - In response to this argument, Naficy's method treats the viruses with ether for 5-30 minutes (Naficy, col. 8, lines 21-31), while Applicant's method treats viruses with ether for one hour. Given the shorter exposure of Naficy's infected blood samples to ether, one would expect that the viral particles of Naficy would not be destroyed, rather reduced in lipid content.
- Applicant argues that Naficy's particles do not expose previously unexposed epitopes. Naficy does not teach or suggest any immunogenic properties of the

partially delipidated viral particles, particularly the initiation of a positive immune response.

- In response to this argument, the Office considers the particles of Naficy and Applicant to be the same. Both are treated with ether, thus delipidated to some degree. One of ordinary skill would expect that the particles exhibit the same properties given their similar methods of production. Absent evidence to the contrary, the particles' functions are expected to be the same.

Conclusion

7. No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications

may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James C. Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.



Stacy B. Chen
September 21, 2005